

Legionnaires Disease: Estimation of Mortality in Traveller's Associated Legionnaires Disease in the Island of Crete

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Introduction

Legionellosis is a bacterial disease caused by bacteria of the *Legionella* genus. In about half of the cases, it develops as a pulmonary disease, with bilateral expansion of the lungs. In terms of clinical manifestations, it is marked by high fever, accompanied by chills, abdominal pain and diarrhoea. The public health significance of the disease is primarily that it has global spread and secondly that water systems, and mainly the hot water systems, air conditioning cooling tanks, humidifiers and other similar systems, are very much like receptors for the bacterium. Furthermore, the mortality rate of *Legionella* infection may reach 40% in hospitalised patients, or even higher in immunodeficient and immunosuppressed patients(1).

Legionellosis and public health

The significance of legionellosis, and specifically Legionnaires' disease, stems from the fact that it is a very severe type of atypical pneumonia with a mortality rate of around 40% if left untreated (with treatment, this rate drops to 0%-11%, depending on the personal medical history of the patients). The rate increases in immunosuppressed patients (around 80%). Furthermore, it is a disease with global spread. The first confirmed epidemic outbreak was recorded in 1957 in the USA. Since then, sporadic cases and microepidemics have been occurring in various parts of the world during all 4 seasons of the year, peaking in summer and autumn. Most *Legionella*-associated pneumonias develop in guests of hotels with central air-conditioning systems. Specifically, 0.5%-5% of community-acquired pneumonias are caused by *Legionella*, while it is estimated that the attack rate of epidemic outbreaks is 0.1%-5% of the general population(1,2).

It is a fact that not enough statistics are collected on Legionnaires' disease on a European level. This is due to the inadequate network of case recordings in the various European Union member states. Based on the recorded evidence, around 20% is associated with travellers, either for leisure or business (travel-associated Legionnaires' disease, TALD). Italy seems to present the most travel-associated cases. Since 2005, around 5,000-6,000 cases of Legionnaires' disease have been reported in the 27 EU member states. Based on these epidemiological

data, the annual mortality rate is around 10%. Interestingly enough, the epidemiological characteristics do not seem to differ much in the USA. However, it is believed that, on the one hand, the actual legionellosis cases are underdiagnosed and, on the other, they are not systematically recorded, resulting in only 1 in 10 actual cases being recorded! (3).

As far back as 2004, the World Health Organization has been implementing a Water Safety Plan, based on the Guidelines for Drinking Water Quality recommended by WHO. European Standard EN 15975-2 and Commission Directive (EU) 2015/1787 amending Council Directive 98/83/EC specify the quality of potable water and the quality of water intended for human consumption in general(2,3).

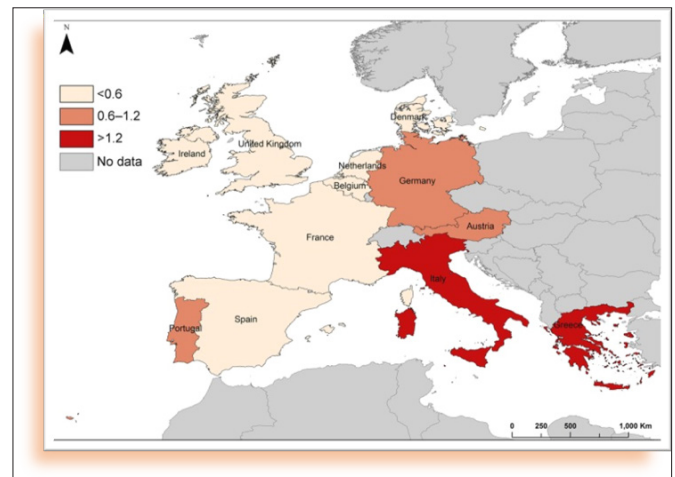


Figure 1: Risk for travel-associated legionellosis, adapted from Julien Beauté, Phillip Zucs, Birgitta de Jong "Risk for Travel -associated Legionnaires' Disease, Europe, 2009", *Emerging Infectious Diseases*, Vol. 18, No. 11, Nov 2012

Preventive Measures

The preventive measures include:

- Keeping the water temperature in the hot water system at 50 °C.

- Cleaning and disinfecting the central air-conditioning cooling tanks periodically. Emptying the water when not in use.
- Using sterile water in hospital ventilators and humidifiers.
- Keeping check on those exposed to identify cases and start treatment early, in the event of an epidemic outbreak.
- Finding the source of contamination in all events. Patients do not need to be placed in isolation or have their secretions disinfected. The start of antimicrobial therapy is necessary(1,4).

Results

Samples from 186 participants were collected. Most participants were men (67.9%) and mean age was 61.9 years (SD=10.4 years) (Table 1). The majority of the samples were collected during autumn (46.8%) or during summer (34.4%).

Information on Cl, pH and temperature of the samples is presented in table 2. The mean number of samples with cl<.2 was 2.78 and of samples with cl .2-1 was 2.39. Also, mostly samples with pH 7.6-8 were collected (mean number being 1.44). As far as temperature is concerned, in most cases temperature between 20 and 25 degrees or between 26 and 30 degrees was recorded.

Overall, 67.7% of the samples was found positive to legionella, with mean number of positive samples being 6.37 (SD=5.66), Table 3. More analytically, 30.1% was found positive to subtype 1, 43.5% to subtypes 2-15 and 44.1% to Spp subtypes. Among positive samples (regardless of the subtype and within each subtype) most positive samples had concentration between 50-1,000 and fewer had a concentration above 10,000.

Fifteen participants (8.1%) died. The association of patients' outcome with their characteristics is presented in table 4. It was found that having cl<.2 (OR=1.21; p=0.002), temperature 26-30 (OR=1.15; p=0.013) or 41-45 (OR=1.57; p=0.002) were significantly associated with greater probability of dying. Also, having more legionella positive samples (regardless of the

subtype) was significantly associated with greater probability of dying (OR=1.12; p=0.004). Furthermore, having more legionella positive samples (regardless of the subtype) with concentration 1,000-10,000 (OR=1.18; p=0.024) or more than 10,000 (OR=1.20; p=0.011) was significantly associated with greater probability of dying. Almost four times greater probability of dying had participants positive in subtypes 2-15 (OR=3.97; p=0.023) or in Spp subtypes (OR=3.87; p=0.025). More analytically, having more legionella positive in subtypes 2-15 samples (regardless the concentration) or having more legionella positive in subtypes 2-15 samples with concentration 1,000-10,000 was significantly associated with greater probability of dying (OR=1.12; p=0.043 and OR=1.21; p=0.043 respectively). In addition having more legionella positive samples in spp subtypes (regardless the concentration) or having more legionella positive samples in spp subtypes with concentration more than 10,000 was significantly associated with greater probability of dying (OR=1.18; p=0.003 and OR=1.38; p=0.005 respectively).

After multiple logistic regression (Table 5), it was found that more positive samples (regardless the subtype) with concentration >10000 was significantly associated with greater probability of dying (OR=1.19; p=.020). Also, having positive samples of Spp subtype was significantly associated with greater probability of dying (OR=3.48; p=.043).

N=186	N (%)
Gender	
female	59 (32.1)
male	125 (67.9)
Age in years, mean (SD)	61.9 (10.4)
Season	
Autumn	87 (46.8)
Winter	3 (1.6)
Spring	32 (17.2)
Summer	64 (34.4)

Table 1: Participants' characteristics

		Death				OR (95% CI)+	P
		No		Yes			
		Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		
Age		61,5 (10,6)		66.8 (7.1)		1.06 (1 – 1.12)	0.058
Gender, N(%)							
	female	56 (94.9)		3 (5.1)		reference	
	male	113 (90.4)		12 (9.6)		1.98 (0.54 -7.31)	0.304
Season, N(%)							
	A u t u m n / Winter	85 (94.4)		5 (5.6)		reference	
	Spring	30 (93.8)		2 (6.3)		1.13 (0.21 – 6.15)	0.885
	Summer	56 (87.5)		8 (12.5)		2.43 (0.76 - 7.8)	0.136
Samples with							
cl	<0.2	2.52 (3.17)	1 (0 – 4)	5.8 (5.67)	3 (0 – 11)	1.21 (1.08 -1.37)	0.002
	0.2-1	2.3 (3.28)	1 (0 – 3)	3.47 (4.9)	2 (0 – 5)	1.08 (0.96 – 1.22)	0.217

	>1	1.61 (2.74)	0 (0 – 2)	3.07 (4.06)	2 (0 – 3)	1.13 (0.99 – 1.29)	0.074
pH	<7	0.15 (0.72)	0 (0 – 0)	0 (0)	0 (0 – 0)	–++	0.998
	7-7.5	0.85 (2.24)	0 (0 – 0)	0.2 (0.56)	0 (0 – 0)	0.7 (0.36 – 1.37)	0.302
	7.6-8	1.4 (2.84)	0 (0 – 1)	1.87 (3.48)	0 (0 – 4)	1.05 (0.89 – 1.24)	0.548
	>8	0.71 (2.33)	0 (0 – 0)	0.6 (1.4)	0 (0 – 0)	0.98 (0.75 – 1.27)	0.852
Temperature	<20	0.67 (1.38)	0 (0 – 0)	0.53 (0.99)	0 (0 – 1)	0.92 (0.6 – 1.42)	0.715
	20-25	3.8 (3.98)	3 (1 – 6)	4.6 (5.11)	4 (0 – 6)	1.04 (0.93 – 1.17)	0.467
	26-30	2.6 (3.33)	1 (0 – 4)	5.4 (6.38)	5 (1 – 8)	1.15 (1.03 – 1.28)	0.013
	35-40	0.82 (1.54)	0 (0 – 1)	1.67 (1.84)	1 (0 – 3)	1.27 (0.99 – 1.64)	0.058
	41-45	0.75 (1.23)	0 (0 – 1)	2.07 (2.25)	2 (0 – 4)	1.57 (1.18 – 2.09)	0.002
	46-50	1.02 (1.6)	0 (0 – 2)	1.87 (2.61)	1 (0 – 4)	1.24 (0.98 – 1.57)	0.079
	51-55	1.13 (1.65)	1 (0 – 2)	1.6 (2.23)	1 (0 – 3)	1.14 (0.88 – 1.47)	0.311
	>56	2.29 (2.87)	1 (0 – 4)	1.27 (1.98)	0 (0 – 3)	0.83 (0.63 – 1.09)	0.176
Total Positive, N (%)							
	No	59 (98.3)		1 (1.7)		reference	
	Yes	112 (88.9)		14 (11.1)		7.38 (0.95 - 57.47)	0.056
Number of total positive		6.03 (5.11)	4 (2 – 8)	9.14 (8.69)	4.5 (2 – 15)	1.12 (1.03 – 1.2)	0.004
Number of total positive: 50-1000		3.11 (2.91)	2 (1 – 4.5)	2.79 (3.75)	2 (0 – 2)	1.06 (0.9 – 1.26)	0.464
Number of total positive: 1000-10000		2.23 (2.93)	1 (0 – 4)	3.5 (4.42)	1.5 (0 – 8)	1.18 (1.02 – 1.35)	0.024
Number of total positive: >10000		1.36 (2.73)	0 (0 – 2)	3.07 (3.83)	2 (0 – 5)	1.2 (1.04 – 1.38)	0.011
Leg1 Positive, N (%)							
	No	62 (88.6)		8 (11.4)		reference	
	Yes	50 (89.3)		6 (10.7)		1.61 (0.55 – 4.77)	0.387
Number of Leg1 positive		3.98 (3.15)	3 (1 – 6)	3.5 (2.74)	3 (1 – 5)	1.04 (0.85 – 1.26)	0.722
Number of Leg1 positive: 50-1000		2.46 (2.05)	2 (1 – 4)	1.33 (1.86)	1 (0 – 1)	0.91 (0.61 – 1.37)	0.657
Number of Leg1 positive: 1000-10000		1.46 (1.46)	1 (0 – 3)	0.83 (1.6)	0 (0 – 1)	0.91 (0.51 – 1.61)	0.735
Number of Leg1 positive: >10000		0.8 (2.16)	0 (0 – 0)	1.33 (1.97)	0.5 (0 – 2)	1.14 (0.85 – 1.54)	0.385
Leg2-15 Positive, N (%)							
	No	101 (96.2)		4 (3.8)		reference	
	Yes	70 (86.4)		11 (13.6)		3.97 (1.21 – 12.97)	0.023
Number of Leg2-15 positive		4.56 (4.15)	3 (1 – 7)	5.45 (6.23)	2 (1 – 13)	1.12 (1.01 – 1.24)	0.043
Number of Leg2-15 positive: 50-1000		2.76 (2.26)	2 (1 – 4)	2.64 (2.84)	2 (1 – 5)	1.16 (0.94 – 1.43)	0.154
Number of Leg2-15 positive: 1000-10000		1.54 (2.62)	0 (0 – 3)	2.45 (3.47)	1 (0 – 6)	1.21 (1.01 – 1.45)	0.043
Number of Leg2-15 positive: >10000		0.91 (2.66)	0 (0 – 1)	0.73 (1.1)	0 (0 – 2)	1.04 (0.81 – 1.34)	0.732
Leg Spp Positive, N (%)							
	No	100 (96.2)		4 (3.8)		reference	
	Yes	71 (86.6)		11 (13.4)		3.87 (1.19 – 12.66)	0.025
Number of Leg Spp positive		4.06 (3.49)	3 (2 – 5)	6.45 (6.06)	6 (1 – 8)	1.18 (1.06 – 1.32)	0.003

Number of Leg Spp positive: 50-1000	1.99 (2.13)	1 (1 – 2)	2 (3.16)	1 (0 – 4)	1.16 (0.93 – 1.45)	0.197
Number of Leg Spp positive: 1000-10000	1.52 (2.37)	1 (0 – 2)	1.73 (2.24)	1 (0 – 3)	1.15 (0.93 – 1.41)	0.199
Number of Leg Spp positive: >10000	0.79 (1.85)	0 (0 – 1)	2.73 (3.8)	1 (0 – 6)	1.38 (1.1 – 1.73)	0.005

Table 2: Patients’ outcome associated with their characteristics

	OR (95% CI)+	P
Number of total positive samples with concentration >10000	1.19 (1.03 - 1.37)	0.020
Leg Spp positive (yes vs no)	3.48 (1.04 - 11.66)	0.043

Table 3: Multiple logistic regression for participants’ outcome, in a stepwise method

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